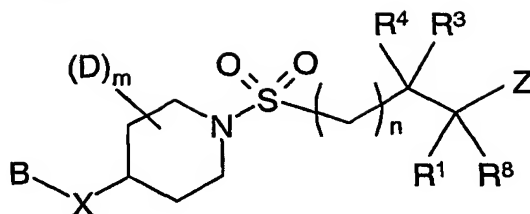


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**CLAIMS:**

What we claim is :-

1. A compound of formula (1):



formula (1)

wherein Z is selected from  $-\text{CONR}^{15}\text{OH}$  and  $-\text{N}(\text{OH})\text{CHO}$ ;

$\text{R}^{15}$  is hydrogen or  $\text{C}_{1-3}$ alkyl;

wherein  $\text{R}^1$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{2-6}$ alkenyl,  $\text{C}_{2-6}$ alkynyl,  $\text{C}_3$ -

$\text{C}_7$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, aryl, heteroaryl and heterocyclyl where the group is optionally

substituted by one or more substituents independently selected from halo, nitro, cyano,

trifluoromethyl, trifluoromethoxy,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{2-4}$ alkenyl,  $\text{C}_{2-4}$ alkynyl,  $\text{C}_{3-6}$ cycloalkyl

(optionally substituted by one or more  $\text{R}^{17}$ ), aryl (optionally substituted by one or more  $\text{R}^{17}$ ),

heteroaryl (optionally substituted by one or more  $\text{R}^{17}$ ), heterocyclyl,  $\text{C}_{1-4}$ alkoxycarbonyl, -

$\text{OR}^5$ ,  $-\text{SR}^2$ ,  $-\text{SOR}^2$ ,  $-\text{SO}_2\text{R}^2$ ,  $-\text{COR}^2$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{NR}^{16}\text{COR}^5$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$  and -

$\text{NR}^{16}\text{SO}_2\text{R}^2$ ;

$\text{R}^{16}$  is hydrogen or  $\text{C}_{1-3}$ alkyl;

$\text{R}^{17}$  is selected from halo,  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl and  $\text{C}_{1-6}$ alkoxy;

$\text{R}^2$  is group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl, heterocycloalkyl, aryl,

heteroaryl, aryl $\text{C}_{1-4}$ alkyl and heteroaryl $\text{C}_{1-4}$ alkyl where the group is optionally substituted by

one or more halo;

$\text{R}^5$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-6}$ cycloalkyl,  $\text{C}_{5-7}$ cycloalkenyl,

heterocycloalkyl, aryl, heteroaryl, aryl $\text{C}_{1-4}$ alkyl and heteroaryl $\text{C}_{1-4}$ alkyl where the group is

optionally substituted by one or more halo;

$\text{R}^6$  is hydrogen,  $\text{C}_{1-6}$ alkyl or  $\text{C}_{3-6}$ cycloalkyl;

or  $\text{R}^5$  and  $\text{R}^6$  together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

wherein  $\text{R}^8$  is hydrogen or a group selected from  $\text{C}_{1-6}$ alkyl,  $\text{C}_{3-7}$ cycloalkyl and heterocyclyl

where the group is optionally substituted by one or more substituents independently selected

from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy and  $\text{C}_{1-4}$ alkyl;

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or R<sup>1</sup> and R<sup>8</sup> together form a carbocyclic or saturated heterocyclic 3- to 6-membered ring;  
wherein R<sup>3</sup> and R<sup>4</sup> are independently hydrogen, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>5-7</sub>cycloalkenyl,  
heterocyclyl, aryl or heteroaryl;

wherein n is 0 or 1;

5 wherein m is 0 or 1;

wherein D is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl or fluoro;

wherein X is  $-(CR^9R^{10})-Q-(CR^{11}R^{12})_u-$  where u is 0 or 1;

Q is O, S, SO or SO<sub>2</sub>;

R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are independently selected from hydrogen, C<sub>1-4</sub>alkyl and C<sub>3-6</sub>cycloalkyl;

10 wherein B is C<sub>2-4</sub>alkenyl or C<sub>2-4</sub>alkynyl, each being optionally independently substituted by a  
group selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, heterocycloalkyl, aryl, heteroaryl, heterocyclyl  
whereby the group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl,  
trifluoromethoxy,  $-CONHR^{13}$ ,  $-CONHR^{13}R^{14}$ ,  $-SO_2R^{13}$ ,  $-SO_2NHR^{13}$ ,  $-SO_2NR^{13}R^{14}$ ,  $-$   
NHSO<sub>2</sub>R<sup>13</sup>, C<sub>1-4</sub>alkyl and C<sub>1-4</sub>alkoxy;

15 R<sup>13</sup> and R<sup>14</sup> are independently hydrogen, C<sub>1-4</sub>alkyl or C<sub>3-5</sub>cycloalkyl;

or R<sup>13</sup> and R<sup>14</sup> together with the nitrogen to which they are attached form a heterocyclic 4 to  
7-membered ring.

or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof.

20 2. A compound according to claim 1 wherein X is  $-(CH_2)-O-$  or  $-(CH_2)-O-(CH_2)-$ .

3. A compound according to claim 1 or 2 wherein B is C<sub>2-4</sub>alkenyl or C<sub>2-4</sub>alkynyl, each  
being optionally independently substituted by C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, aryl, heteroaryl or  
heterocycloalkyl.

25

4. A compound according to any one of claims 1 to 3 wherein R<sup>1</sup> is hydrogen, C<sub>1-6</sub>alkyl  
or aryl where C<sub>1-6</sub>alkyl or aryl are optionally substituted by one or more substituents  
independently selected from C<sub>1-4</sub>alkyl, aryl (optionally substituted by R<sup>17</sup>) and heteroaryl  
(optionally substituted by R<sup>17</sup>) and wherein R<sup>17</sup> is halo or C<sub>1-4</sub>alkyl.

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5. A compound according to any one of claims 1 to 4 for use as a medicament.

6. The use of a compound according to any one of claims 1 to 4 in the manufacture of a  
5 medicament in the treatment of a disease condition mediated by one or more metalloproteinase enzymes.

7. The use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament in the treatment of a disease condition mediated TNF $\alpha$ .

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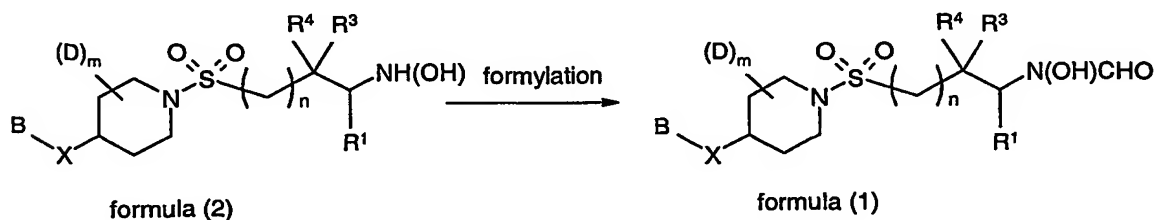
8. A method of treating autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound according to claim 1.

15

9. A pharmaceutical composition comprising a compound according to any one of claims 1 to 4; and a pharmaceutically-acceptable diluent or carrier.

10. A process for preparing a compound according to claim 1 comprising, when Z is –  
20 N(OH)CHO, the step of:

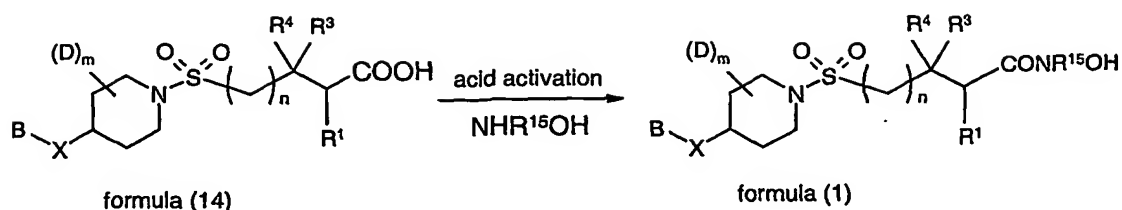
a) converting a hydroxylamine of formula (2) into a compound of formula (1);



or when Z is –CONR<sup>15</sup>OH, the step of:

25 b) converting an acid of formula (14) into a compound of formula (1);

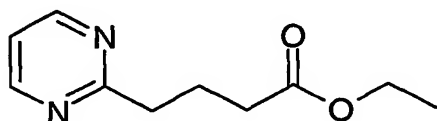
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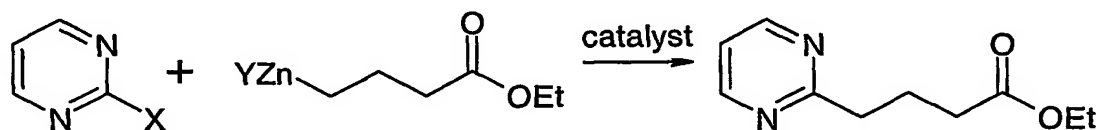
and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- 5 iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.

11. Ethyl 4-(pyrimidin-2-yl)butanoate.



- 10 12. A process comprising the reaction of a 2-halopyrimidine, 2-tosylpyrimidine, 2-pyrimidinyl triflate or 2-pyrimidinyl mesylate with 4-ethoxy-4-oxo-butylzinc bromide or 4-ethoxy-4-oxo-butylzinc iodide in the presence of a catalyst;



wherein X is halo, triflate or mesylate and Y is bromide or iodide.

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13. A process according to claim 11 wherein the catalyst is generated from bis(acetonitrile) palladium (II) dichloride and triphenylphosphine.

14. The use of bis(acetonitrile) palladium (II) dichloride and triphenylphosphine in a  
20 Negishi coupling reaction.